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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/751,292	01/02/2004	Mark A. Hoffman	CRNC.107055	1596

46169 7590 10/09/2007

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EXAMINER
SKOWRONEK, KARLHEINZ R

ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
10/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/751,292	HOFFMAN ET AL.	
	Examiner	Art Unit	
	Karlheinz R. Skowronek	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 32-52 are pending.

Claims 1-31 are cancelled.

Claims 32-52 are being examined.

Claim Rejections - 35 USC § 112

Response to Arguments

Applicant's arguments, see p. 9, filed 16 July 2007, with respect to the rejection of claims 37,38,40,47, and 51-52 under 35 USC 112, 2nd paragraph have been fully considered and are persuasive. The rejection of claims 37,38,40,47, and 51-52 under 35 USC 112, 2nd paragraph has been withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The following rejection is reiterate from the previous office action.

Claims 32-52 rejected under 35 U.S.C. 102(b) as being anticipated by Kobrinskii et al (Biomedical Engineering, Vol. 31, No. 3, p. 172-174), as evidenced by Steadman's Medical Dictionary (entries for heredity and inheritance, 2000).

The claims are directed to a method (claims 32-40 and 49-52) and system (claims 41-48) of determining the probability that the a person has a gene mutation by receiving a request for genetic test results for a patient; querying a database for the results; if the genetic test results do not exist, obtain the route of inheritance for the gene; query a database to identify any family members with genetic test results with the route of inheritance; use the genetic results of the identified family members to calculate the probability that the patient has a gene mutation; report the probability that the patient has a gene mutation.

Kobrinskii et al teach a system/method with the limitations of the instant claims. The system of Kobrinskii et al makes use of a national healthcare database (cl. 33, 42, 40) to provide the likelihood of gene mutations in individuals. Queries of the first and second database to obtain information regarding the individual and the individuals family to present a calculated likelihood the individual has a gene mutation (p. 172, para. 7-8) or has a mutation that could indicative of genotoxic environmental factors (interpreted as atypical events) (p. 172, para 2) (cl. 37, 38, 46, 47, 51, and 52) are taught by Kobrinskii et al. The teaching control of dispensary observations by Kobrinskii et al also reads on the limitation of cl. 48 of queries occurring in response to an order for medication (p. 172, para 2). Kobrinskii et al teach the system also contains an algorithm for compiling medical conclusions that are based on analysis of the database information including pedigree/genealogical tree (p. 172, para. 6) reading on claims 32, 34, 35, 41, 43, 44, and 49. The method instructions are embodied in at least 1 computer readable media, reading on claims 36 and 50 (p. 172, para 3). Kobrinskii et al teach the

calculation of the type of heredity (p. 172, para 7) prognosis of the risk of inherited diseases in a given family reading on claim 39 and 48, modes of inheritance (p. 172, para 2).

Response to Arguments

Applicant's arguments filed 16 July 2007 have been fully considered but they are not persuasive. Applicant argues Kobrinskii et al do not teach receiving requests for test results and automatically calculating the likelihood of having a mutated gene based on the person's mode of inheritance.

With respect to the argument that Kobrinskii et al does not teach receiving requests for test results, Kobrinskii et al shows on page 172 that the software allows the direct accessing of a patients medical data from a patients medical card containing, among other information, clinical examination and laboratory analysis. The recitation of direct access demonstrates that the patients data is queried, although the exact wording is not present in the teaching, the concept of querying is presented throughout the Kobrinskii reference. The use of databases whether as a personal medical card or as a regional genetic register inherently employs the use of queries in order to obtain information from the database.

With respect to the argument that Kobrinskii et al does not show automatically calculating the likelihood of having a mutated gene based on the person's mode of inheritance, it is noted that the features upon which applicant relies (i.e., automatic calculation of risk after the system is prompted for test results) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification,

limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Kobrinskii et al shows the calculation of likelihoods, ie risk. Specifically, Kobrinskii et al shows on p. 172 that "mathematical models of the risk of genetic diseases implement program modules for calculating the type of heredity, risks of specific diseases, karyotype analysis, etc. The software also includes an expert database and a system for visual analysis of chromosome defects. Automatic analysis of genealogical trees includes formation of medical conclusion of the risk of genetic disease in given patient and on the specificity of genetic predisposition of the disease."

With respect to the argument that Kobrinskii et al doe not show a receiving module or a presenting module, Kobrinskii et al shows that a Microsoft SQL server is employed to provide the database access anticipating the receiving and presenting modules.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Rejection of claims 32-52 as obvious over Coulson et al.

Response to Arguments

Applicant's arguments, see p. 15-17, filed 27 June 2007, with respect to the rejection of claims 32-52 as obvious over Coulson et al. have been fully considered and are persuasive. The rejection of claims 32-52 as obvious over Coulson et al. has been withdrawn.

The following rejection is reiterated from the previous office action.

Claims 32-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pathak et al (Proceedings of the Tenth Conference on Artificial Intelligence for Applications, p. 164- 170, March 1994).

The claims are directed to a method (claims 32-40 and 49-52) and system (claims 41-48) of determining the probability that the a person has a gene mutation by receiving a request for genetic test results for a patient; querying a database for the results; if the genetic test results do not exist, obtain the route of inheritance for the gene; query a database to identify any family members with genetic test results with the route of inheritance; use the genetic results of the identified family members to calculate the probability that the patient has a gene mutation; report the probability that the patient has a gene mutation.

Pathak et al teach a computerized method and system for automatically reporting genetic risk, i.e. the probability of a gene mutation. The method of Pathak et al relies on case data for a patient.The system analyzes the data and produces a probability of the presence of a mutation. The input of case data as depicted in fig. 1 conceptually demonstrates data that is stored and utilized by the system, thereby reading on the limitation of a database. Consistent with the limitation of a database is the blackboard (p.165, col. 2, para. 1), a global data structure. Pathak et al teach the input as a set of objects each having the attributes name, sex, parents, siblings, spouse, children, loci (p.165, col. 2, para. 1). The attribute *loci*, as Pathak et al teach, is a set of alleles in the genome reading on the limitation of genetic test results (p.165, col. 2, para. 1). Pathak et al teach the use of rule sets to define queries of the case data to identify the route of inheritance based on familial relationships as well as to utilize the loci information to calculate a probability of an allele's presence (p.165, col. 2, para. 2 and p. 166, col. 2, #8). Pathak et al shows genetic risks influence medical decisions (p. 169, col. 2).

Pathak et al does not teach risk of atypical events.

It would have been obvious to apply the method/system of Pathak et al to practice the instant invention because a clinician would want to know what the probability is that a mutation is linked or correlated with an event that is not typical for the condition and because the method/system of Pathak et al is modular (p. 169, col 2, para 1). Further, it would be obvious for a clinician to inquire the risk associated with having an adverse reaction to a prescribed treatment. This is a function that every clinician performs each time a treatment for a condition is prescribed. For example, such as queries related to allergies to specific antibiotics like sulfadrugs or to particular general anesthetics. As with every treatment, it is common sense that a clinician would first determine if a condition exists in a patient through examination, diagnostic tests in order to prescribe potential modes of treatment, then consults (queries) the family history for previous instances of the condition under a defined genetic background. After considering the family history, the clinician then determines given the genetic background of the patient which prescribed mode of treatment yields the lowest risk of adverse reaction. The limitation of querying the patient record/database and the family history record/database upon prescription of medication merely automates a common process of the medical arts and is therefore obvious.

One would have been motivated to do so because Pathak et al teach the method/system allows the study of any given case with any number of observations and assumptions (p. 169, col 1, para 1), the system streamlines the computation of risk which are used to make critical medical decisions (p. 169, col 2, para 2) and

method/system automates error-prone, complex, tedious process to be a valuable aid to clinicians(p. 164, col.1, para. 1).

Regarding claims 34 and 43, Pathak et al teach knowledge source 2 concerned with allele inheritance relations with in the pedigree (p. 165, col. 2, "allele flow").

Regarding claims 35 and 44, Pathak et al teach calculating a likelihood the individual has a mutated form of the gene using the genetic markers (alleles) of at least one family member (p. 166, col. 2, "possible–explanations" and "Bayesian-analysis").

Regarding claim 36, Pathak et al teach a computer readable media comprising the instructions for the method (p. 169, col. 2, para 2, "software").

Regarding claims 37 and 46, the determination of gene variant that is indicative of atypical event is taught by Pathak et al in light of the statement that genetic risk is computed by considering disease characteristics (p. 164, col 1, para 1, lines 4-6). Response to treatment or therapy is view to be an example of a disease characteristic, For example, the response or lack of response of breast cancer to taxol treatment is a characteristic of the disease. The application of rule 6 (p. 166, col. 2) to the data would result in the determination of previous atypical event that had occurred in any members 'of the family because rule 6 is directed to determining observable events. Since an atypical event is observable, rule 6 can be used to determine if a genetic variant is indicative of an atypical event.

Regarding claims 38 and 47, presenting an alert to a user, if the gene variant is indicative of an atypical event, Pathak et al teach rule 9 (p. 167, col. 1, "system-output"). The teaching of rule 9 reads on presenting an alert to the user since the output can be

modulated by the user, for example to provide explanations for probabilities that exceed a threshold value

Regarding claim 39 and 48, Pathak et al teach the example of x-linked mode of inheritance (p. 167, col. 1, "X-linked").

Regarding claims 33, 40, 42 and 45, Pathak et al teach that all a user must do is provide the system with the relevant data (p. 169, col 1., last three lines). It is common for an individual's medical information to exist in electronic form and comprise medical data of related family members. Therefore the teaching of providing the system with the relevant data is viewed to read on the limitations of electronic records from a comprehensive healthcare database.

Regarding claims 49-52, the limitations are taught in part as above.

Response to Arguments

Applicant's arguments filed 16 July 2007 have been fully considered but they are not persuasive. Applicant argue that Pathak et al. does not show the limitations of receiving request for test results of a mutated gene for a patient, querying a database for the result and calculating a likelihood. The argument is not persuasive because Pathak et al. shows a system for automatically computing genetic risks. The limitations recited by applicant are taught in Pathak et al. With respect to the limitation of receiving a request for genetic test result is an inherent limitation Pathak et al. To evidence the inherent nature of the request for genetic test results, Pathak et al shows genetic counselors consider a variety if data, including family history, disease characteristics and DNA information (abstract). Pathak et al define genetic risk as the probability (i.e.

likelihood) that patients may either develop a genetic disorder or transmit a genetic disease to their children (p. 164). Pathak et al shows that the status of some members may be unknown and these are the people for whom a risk figure is typically desired (p. 164, col. 2). The statement is interpreted to show the inherency of receiving a request of test results, querying a database for results and if the results do not exist to calculate a genetic risk. The limitation of querying a database is present in Pathak et al to the extent that Pathak et al describes inputting the case data to the system (p. 164, col. 1). Pathak et al shows that the system has a user-interface that facilitates interaction between the genetic counselor to obtain case data. Therefore, Pathak makes the invention of independent claims 31, 41 and 49 obvious. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., automatic calculation of risk after the system is prompted for test results) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). With respect to applicant assertion of official notice, official notice was not taken, rather an explanation of the obviousness of Pathak et al was provided.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karlheinz R. Skowronek whose telephone number is (571) 272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

1 October 2007

/KRS/
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JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER